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TITLE: Detection of Early lung Cancer Among Military Personnel (DECAMP)

PRINCIPAL INVESTIGATOR: Avrum E. Spira, MD

CONTRACTING ORGANIZATION: Boston University
Boston, MA 02118

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Avrum E. Spira, MD
Emily Maple, MPH

E-Mail: emaple@bu.edu

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**14. ABSTRACT**

The purpose of this work is to develop and validate molecular biomarkers found in blood, tissues, or other bodily fluids, which may be used for the early detection of lung cancer among military personnel and veterans. Over the course of the fifth year of this award, we have made significant progress towards enrollment in both clinical trials. We have recruited ~60% of the 500 total subjects in the indeterminate pulmonary nodule study (Protocol 1), and ~40% of the 800 total subjects in the longitudinal screening study (Protocol 2). We have ensured that every effort is made to obtain high quality specimens from airway brushings, nasal brushings, and frozen airway biopsy samples. We held our third annual DECAMP consortium meeting in Chicago, IL, including one day of RA-specific meetings. Designated committees meet regularly including the Steering, Adjudication, and Biomarker Committees as well as Imaging and Biostatistics/Analysis Working Groups. Most notably, significant validation work has begun on the Genomics and Proteomics Biomarkers. Finally, we have continued to identify additional funding sources both to supplement infrastructure support within DECAMP and pursue additional biomarker studies.

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**Table of Contents**

Introduction:

The purpose of this work is to develop and validate molecular biomarkers that may be used for the early detection of lung cancer. By recruiting approximately 500 patients with indeterminate pulmonary nodules from Military Treatment Facilities and Veteran's Administration Hospitals, DECAMP plans to identify 75 patients with lung cancer for our molecular studies. For the study to develop tests that can identify the patients at highest risk for having or developing lung cancer, DECAMP will recruit approximately 800 high-risk current and former smokers from these same hospitals, determine whether they have lung cancer now and then follow them annually for up to four years to determine if they develop lung cancer. We expect to identify 50 patients who did not have cancer when they join the study, but develop lung cancer while they are being monitored. The clinical applications of this study will come from the development of tests to more accurately diagnose disease at an early potentially curable stage but also predict the occurrence of lung cancer in the future. Additionally, these biomarkers found in blood, other body fluids, or tissues will be collected more easily and are less invasive than surgery. Non-invasive collection of biological samples will be less painful for the patient and allow easier and more frequent monitoring of disease. The intent of this research is to develop early detection strategies that will ultimately decrease lung cancer deaths. This will improve the health and welfare of the military, and the American public as a whole.

During the fifth year of the DECAMP consortium, we have made significant progress toward the Specific Aims of the grant. Specifically, recruitment of subjects into both clinical trials has continued to improve steadily (see Figures 1-2 and tables 1-4). The RA Team has met with increased frequency (bi-weekly) over the past year with each RA continuing to collect information contained in the screening logs. While continuing recruitment into both protocols, RAs are also responsible for the follow-up and scheduling of DECAMP-2 follow-up visits for years 1 and 2. This has significantly increased the workload for sites that recruit heavily into DECAMP-2. Because data entry continues to be a top priority, we have hired an additional part time RA in response to data entry issues at the top recruiting MTF sites, which has helped to decrease the burden of missing data and improve the overall quality of the data. There was also an RA-specific meeting prior to the consortium-wide DECAMP meeting in Chicago that addressed site specific concerns related to patient recruitment, data collection and biospecimen processing.

Beyond progress towards patient enrollment, we continued to evaluate the quality and quantity of RNA in bronchial brushings (n=287; mean: 6.4; range: 2.1-9.4), nasal brushings (n=52; mean: 4.2; range: 2.3-10), and bronchial biopsies (n=40; mean: 3.3; range: 1.1-7.1) for each site (Table 11). In those sites with lower yields and poor quality, we provided feedback and reviewed protocol for sample collection. Currently, there are a total of 13,388 samples on 577 subjects banked at the Biorepository of Boston University and there are additional samples pending shipment from individual sites.

One of the major milestones achieved over past 12 months was the initial validation of candidate molecular biomarkers in the airway and blood within DECAMP1. As of the first quarter of the 5$^{th}$ year, the adjudication committee had completed adjudication on 91 cases and controls that were used for the initial phase of biomarker validation. (We plan to have a second wave of biomarker validation studies on larger numbers of cases and controls within year 6). Bronchial airway brushing specimens were processed at the BU (Genomics) Core for RNA isolation, microarray hybridization and analysis of the 23-gene biomarker (Silvestri et al NEJM 2015); while plasma samples were processed at the Vanderbilt (Proteomics) Core for ELISA of three candidate proteins: C4C, CRP, and CYFRA. Biomarker scores were derived for each sample at both cores and then sent to the Biostatistics Core at Brown University for biomarker performance evaluation. For the 23-gene bronchial biomarker, the initial validation results on all cases and controls with final diagnoses showed sensitivity 82% (95% CI: 70-91%), and specificity 47% (95% CI: 23-72%), results that closely mirror the performance of this biomarker in the AEGIS trials (Silvestri et al. NEJM 2015). For the plasma biomarkers, the initial validation results showed that for C4C the sensitivity was 2% (95% CI: 0-10%) and specificity was 84% (95% CI: 60-97%); for CRP the sensitivity was 27% (95% CI: 16-40%) and the specificity was 89% (95% CI:67-99%); and for CYFRA the sensitivity was 66% (95% CI: 52-78%) and specificity was 58% (95% CI: 34-80%). Given the weak performance of the individual plasma markers, the plasma biomarkers will be combined with imaging-based markers for all future validation studies.

We continue to explore future funding opportunities for the DECAMP Consortium. We have successfully negotiated a four-year contract with Janssen Pharmaceuticals which will help support infrastructure of DECAMP as well as additional biomarkers, both in lung cancer and COPD. As a result of this additional funding, we have added three years of follow up to patients diagnosed with cancer and one additional time point for noninvasive biospecimen collection.

We held a consortium-wide, in-person meeting in Chicago, IL, in May 2016 to discuss the current state of DECAMP and future directions for the group. Similar to the previous year, we used a portion of the time together to break into smaller groups: clinical, imaging, and molecular. Through these groups we strategized how to manage current issues as well as brainstorm on future directions. One of the recommendations was to work on an imaging biomarker, which has since been implemented and is actively underway. There was also a strong consensus that the consortium should initiate biomarker

discovery projects.

Other accomplishments of the year are included in the summary of our progress related to each of the tasks in our SOW as specifically outlined below.

**Task 1 Clinical Trial Accrual**

**Project 1 – Accrual Target 500 total subjects: Within that cohort, we will match lung cancers/controls for the biomarker studies**
**Biospecimen collection: blood, endobronchial biopsies, nasal brushings, bronchial brushings, buccal scrapings, sputum, urine**
**Current Accrual: See Tables 1 & 3**

**Project 2 – Accrual Target 800 total subjects: Within that cohort, we will match lung cancers/controls for the biomarker studies**
**Biospecimen collection: blood, endobronchial biopsies, nasal brushings, bronchial brushings, buccal scrapings, sputum, urine**
**Current Accrual: See Tables 2 & 4**

**1a. Clinical site Accrual:** Based on accrual rates, the projected accrual over the 12 month No-Cost Extension is outlined in the graph below. In order to maintain or exceed these rates, the Coordinating Center will work closely with each site to reach these targets using goal-setting, recruitment tactics, and screening logs

| Site | DECAMP-1 | DECAMP-2 |
|---|---|---|
| **Boston VA** | 17 | 20 |
| **Dallas VA** | 5 | 2 |
| **Denver VA** | 3 | 11 |
| **LA VA/UCLA** | 6 | 26 |
| **Nashville VA Medical Center** | 5 | 14 |
| **Philadelphia VA/Upenn** | 21 | 4 |
| **Pittsburgh VA** | 5 | 0 |
| **Roswell Park Cancer Center** | 0 | 3 |
| **Brooke Army Medical Center** | 10 | 0 |
| **Naval Medical Center Portsmouth** | 6 | 16 |
| **Naval Medical Center San Diego** | 12 | 26 |
| **Walter Reed National Military Medical Center** | 18 | 38 |
| **Total** | **108** | **160** |

**1b. Samples collected:**

| Biosamples | Quantity | Analytes | Project 1 Diagnostic | Project 2 Screening |
|---|---|---|---|---|
| **Blood*** | 50 mL | Protein/RNA/DNA | Plasma CD4 Protein | ------- |
| **Blood*** | 50 mL | RNA | Exosomal miRNA | ------- |
| **Endobronchial Biopsies via Bronchoscopy** | 6 biopsies** | Protein/RNA/DNA | ------- | ------- |
| **Endobronchial Brushings via Bronhcoscopy** | 1 brush | RNA | 23 Gene Expression Marker | ------- |
| | 1 brush | Protein | ------- | ------- |
| | 1 brush | DNA | ------- | ------- |
| **Nasal Brushings** | 2 brushes | RNA | ------- | Gene expression profiling |
| **Buccal Scrapings** | 1 brush | RNA | ------- | ------- |
| **Sputum** | ------- | DNA | ------- | ------- |
| **Urine** | 25 mL | Metabolomics | 4 Metabolite Marker | ------- |
| **Tumor Tissue***** | ------- | DNA/RNA | ------- | ------- |

*** Plasma, Serum, and PAXGene**

**** 2 biopsies are obtained from three subsegmental carinas (RUL, LUL, RML)**

***** Paraffin and fresh frozen tissue where available**

**1c. Core Labs**

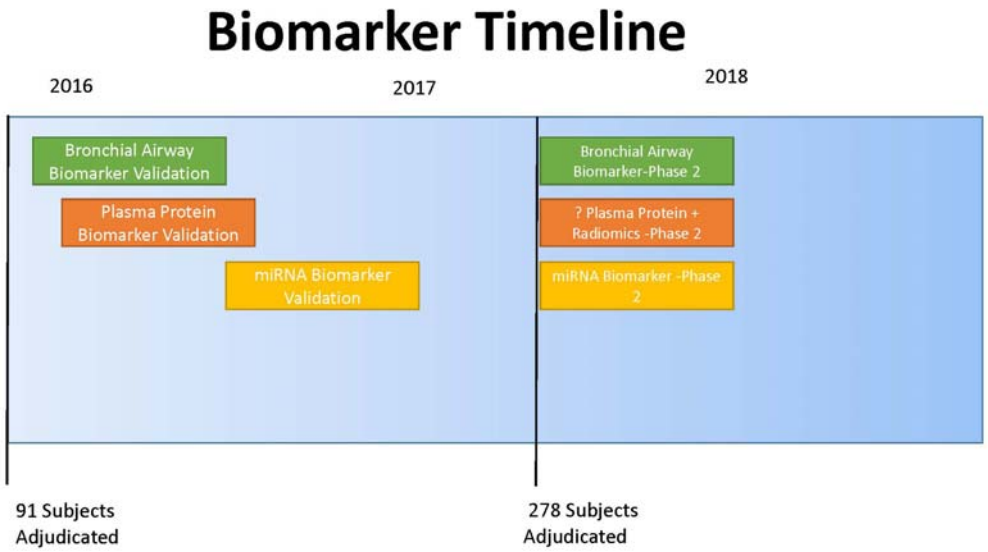
- **Biorepository:** The Biorepository Core will continue to receive, store, and track all biospecimens in the DECAMP Consortium. Ms. Spencer will provide Ms. Maple with a spreadsheet, updated monthly, of all specimens being housed in and pulled from the Biorepository Core at BU.
  Ms. Spencer continues to provide a spreadsheet, updated monthly. Please see Table 13 for updated sample numbers.
- **Pathology:** The Pathology Core at MD Anderson will continue to store all ambient samples provided by clinical sites of bronchial biopsy and surgical tissue. MD Anderson will also continue to process formalin-fixed samples

MD Anderson continues to provide a spreadsheet, updated monthly.

- **Biostatistics:** The Biostatistics Core at Brown University will continue to maintain the database and provide support for biomarker analysis.
  The Biostatistics Core at Brown holds biweekly biomarker analysis meetings to update progress on biomarker analysis and manuscript writing.

**Task 2 Biomarkers**

**2a Validation**




- Bronchial Airway gene-expression Biomarker: We have successfully validated a 23 gene airway biomarker in ~90 DECAMP-1 subjects to date from (phase 1). We plan to validate this biomarker in an additional set of at ~190 subjects from DECAMP-1 in Summer 2017 (phase 2) which will complete this biomarker work
  During FY5 the first round of biomarker validation was performed on 90 subjects (one-third no cancer, two-thirds cancer). The validation results were presented initially at the January EAB Meeting and then in more detail at the May EAB Meeting. See Table 14.
- Plasma Protein Biomarker: We have attempted to validate three protein markers in the serum of the same 90 subjects: C4d , CRP and CYFRA21. We plan to validate these markers on an additional set of ~190 subjects and integrate with radiomic markers on these same subjects in the Summer 2017
  The Plasma Protein Biomarker was presented at the May 2016 EAB Meeting and is in the process of combining the biospecimen marker with the radiomics marker.
- Molecular: We are in the process of prevalidating an exosomal miRNA signature in blood. We plan to do an initial validation on the first 90 subjects in the Winter 2016 with a second phase of validation in Summer 2017
  The first round of validation for the molecular signature in plasma will be presented at the January 2017 EAB Meeting.

**2b Biomarker Discovery**

We plan to sequence mRNA from the nasal epithelium on ~100 subjects in DECAMP-1 to refine and validate an existing nasal gene-expression biomarker for lung cancer diagnosis in Spring 2017. We also plan to do RNA-seq on endobronchial biopsies from cases and controls within DECAMP 1 in

order to define the immune-related changes within the “field of injury” of smokers who develop lung cancer

**Task 3 DECAMP Committees**

- Steering Committee: meets bi-monthly; meetings continued on a bi-monthly basis
- Adjudication Committee: meets as needed; continuous adjudication being processed
- Biomarker Committee: meets as needed; generally 2-3 times within a month depending on when biomarkers are being proposed; Biomarker Committee meetings are held at least bi-monthly and most recently to discuss projected biomarker progress during the No Cost Extension year.
- Biostatistics Committee: meets biweekly on Mondays at noon (EST); Biostatistics Committee (mentioned above) continues to meet
- Imaging Working Group: meets monthly; initiated by ACRIN, the Imaging Group meets monthly and is run by Dr. Denise Aberle and Dr. Caroline Chiles
- Publication Committee: begin official meetings Fall 2016 (once first draft of first paper is completed August 2016); formulations of publication ideas are being formulated and meetings for the publication committee begin January 2017
- Data Access Committee: begin official meetings Fall 2016; ACRIN will be heading the Data Access Committee Meetings beginning January 2017

# DECAMP-1 (ACRIN 4703)

**Table 1: DECAMP 1 Cumulative Accrual**

**Cumulative Accrual Yr 1 through Yr 5 - (Jan 2013 - Sept 2016)**
**tient Accrual by Every Submitting Institution : 4703**

| ACRIN | |
|---|---|
| Walter Reed National Military Medical Center | 60 |
| VA Boston Healthcare System | 50 |
| Brooke Army Medical Center | 35 |
| Naval Medical Center San Diego | 35 |
| Phila/Veterans Administration Hosp | 29 |
| Hospital of the University of Pennsylvania | 29 |
| VA Greater Los Angeles Health Care System | 18 |
| Naval Medical Center Portsmouth | 18 |
| VA North Texas Health Care System | 14 |
| Nashville VA Medical Center | 13 |
| VA Pittsburgh Healthcare System | 12 |
| VA Eastern Colorado Health Care System | 6 |
| **TOTAL :** | **319** |
| **GRAND TOTAL :** | **319** |

**Figure 1: DECAMP 1 Cumulative Accrual: January 2013 - September 2016**

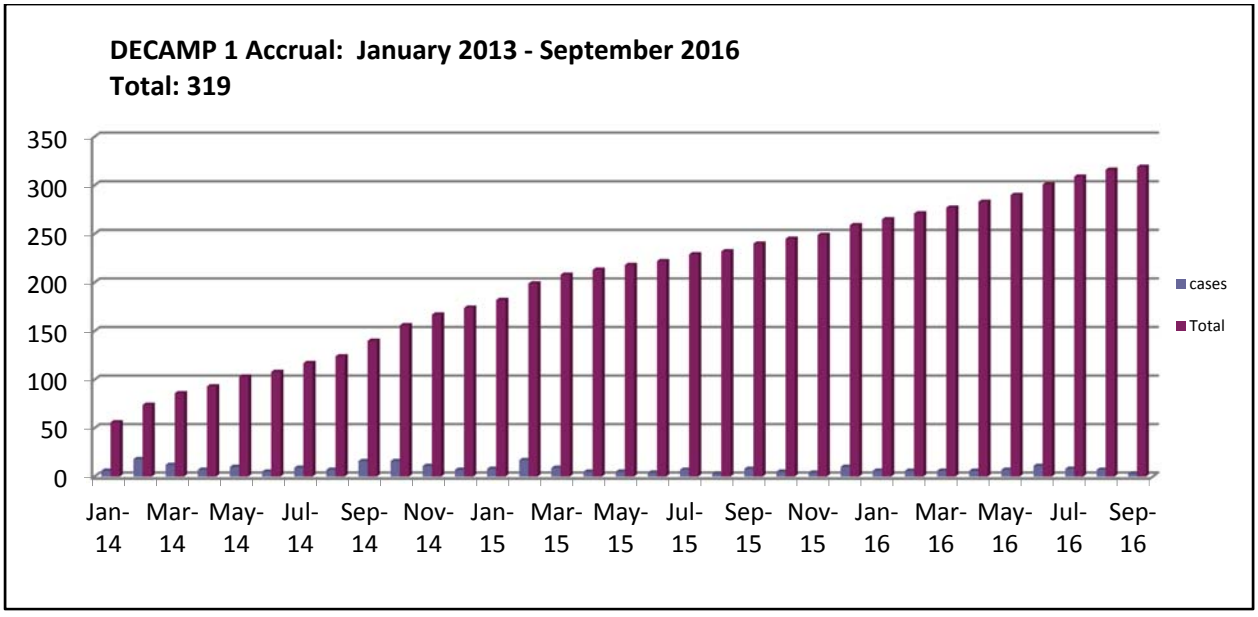


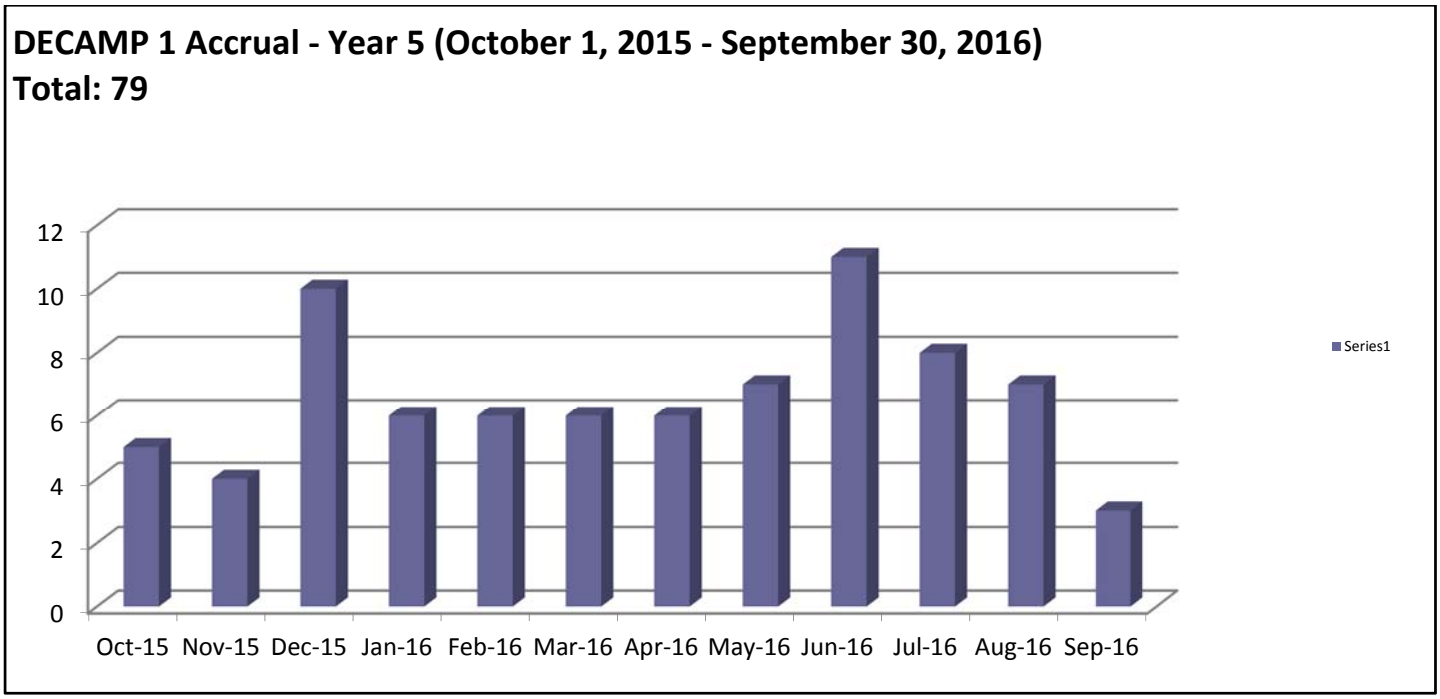
**Table 2: DECAMP 1 Accrual Year 5 (Oct 2015 – Sept 2016)**

**Year 5 Accrual (Oct 2015 - Sept 2016)**

**Patient Accrual by Every Submitting Institution : 4703**

| ACRIN | |
|---|---|
| Walter Reed National Military Medical Center | 15 |
| VA Boston Healthcare System | 14 |
| Phila/Veterans Administration Hosp | 11 |
| Hospital of the University of Pennsylvania | 9 |
| Naval Medical Center San Diego | 9 |
| VA Greater Los Angeles Health Care System | 6 |
| Brooke Army Medical Center | 6 |
| Nashville VA Medical Center | 5 |
| Naval Medical Center Portsmouth | 3 |
| VA North Texas Health Care System | 1 |
| **TOTAL :** | **79** |
| **GRAND TOTAL :** | **79** |

**Figure 2: DECAMP 1 Accrual Year 5 (Oct 2015 – Sept 2016)**



## DECAMP 2 (ACRIN 4704)

### Table 3: DECAMP 2 Cumulative Accrual

**Cumulative Accrual Yr 2 through Yr 5 - (Nov 2013 - Sept 2016**
**tient Accrual by Every Submitting Institution : 4704**

| ACRIN | |
|---|---|
| Walter Reed National Military Medical Center | 86 |
| VA Greater Los Angeles Health Care System | 65 |
| Naval Medical Center San Diego | 60 |
| Nashville VA Medical Center | 34 |
| Naval Medical Center Portsmouth | 33 |
| VA Boston Healthcare System | 32 |
| VA Eastern Colorado Health Care System | 28 |
| Brooke Army Medical Center | 9 |
| Hospital of the University of Pennsylvania | 7 |
| Roswell Park Memorial Institute | 4 |
| VA North Texas Health Care System | 1 |
| TOTAL : | 359 |
| GRAND TOTAL : | 359 |

### Figure 3: DECAMP 2 Cumulative Accrual: November 2013 - September 2016

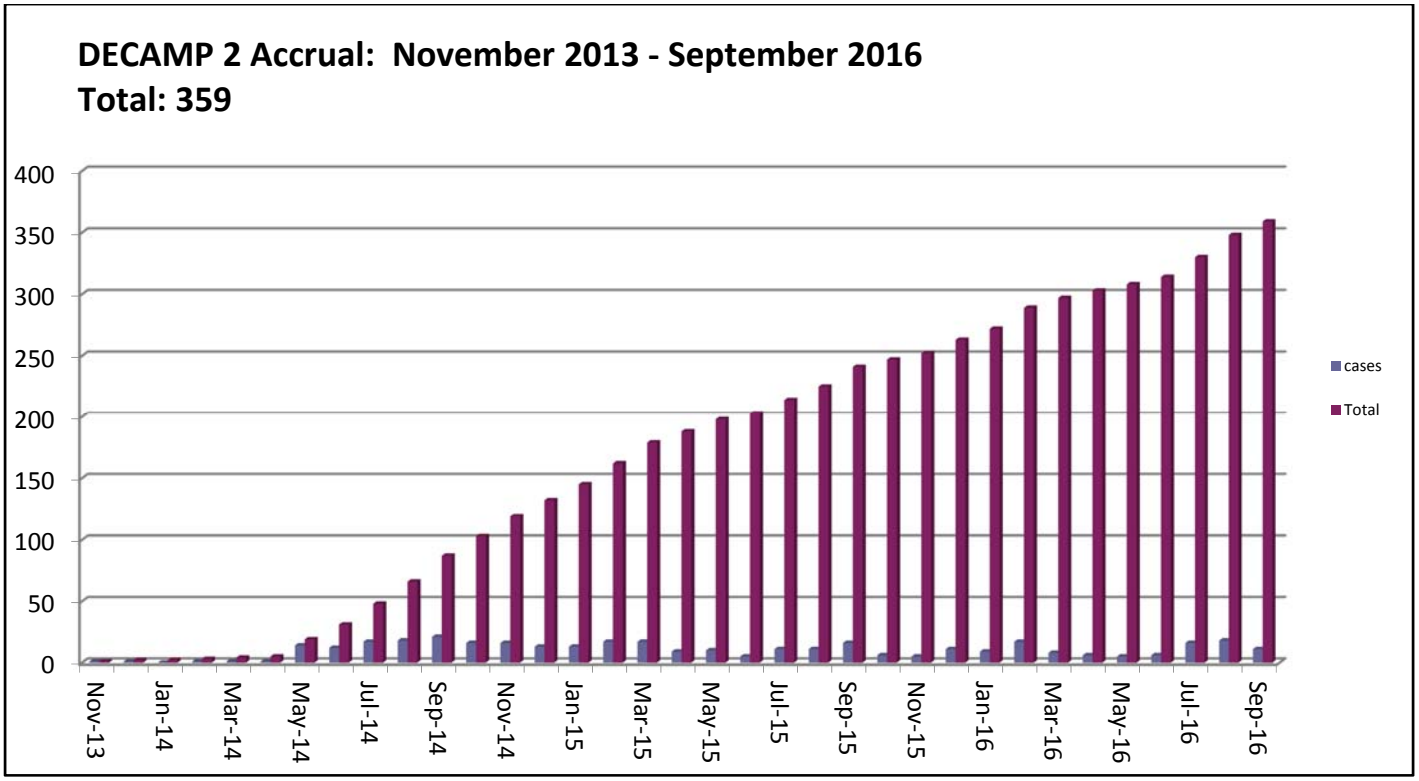


**Table 4: DECAMP 2 Accrual Year 5 (Oct 2015 – Sept 2016)**

**Year 5 Accrual (Oct 2015 - Sept 2016)**

**atient Accrual by Every Submitting Institution : 4704**

| ACRIN | |
|---|---|
| VA Greater Los Angeles Health Care System | 29 |
| Walter Reed National Military Medical Center | 19 |
| VA Boston Healthcare System | 15 |
| Nashville VA Medical Center | 15 |
| VA Eastern Colorado Health Care System | 14 |
| Naval Medical Center San Diego | 13 |
| Naval Medical Center Portsmouth | 11 |
| Brooke Army Medical Center | 2 |
| **TOTAL :** | **118** |
| **GRAND TOTAL :** | **118** |

**Figure 4: DECAMP-2 Accrual: Year 5 (Oct 2015 – Sept 2016)**

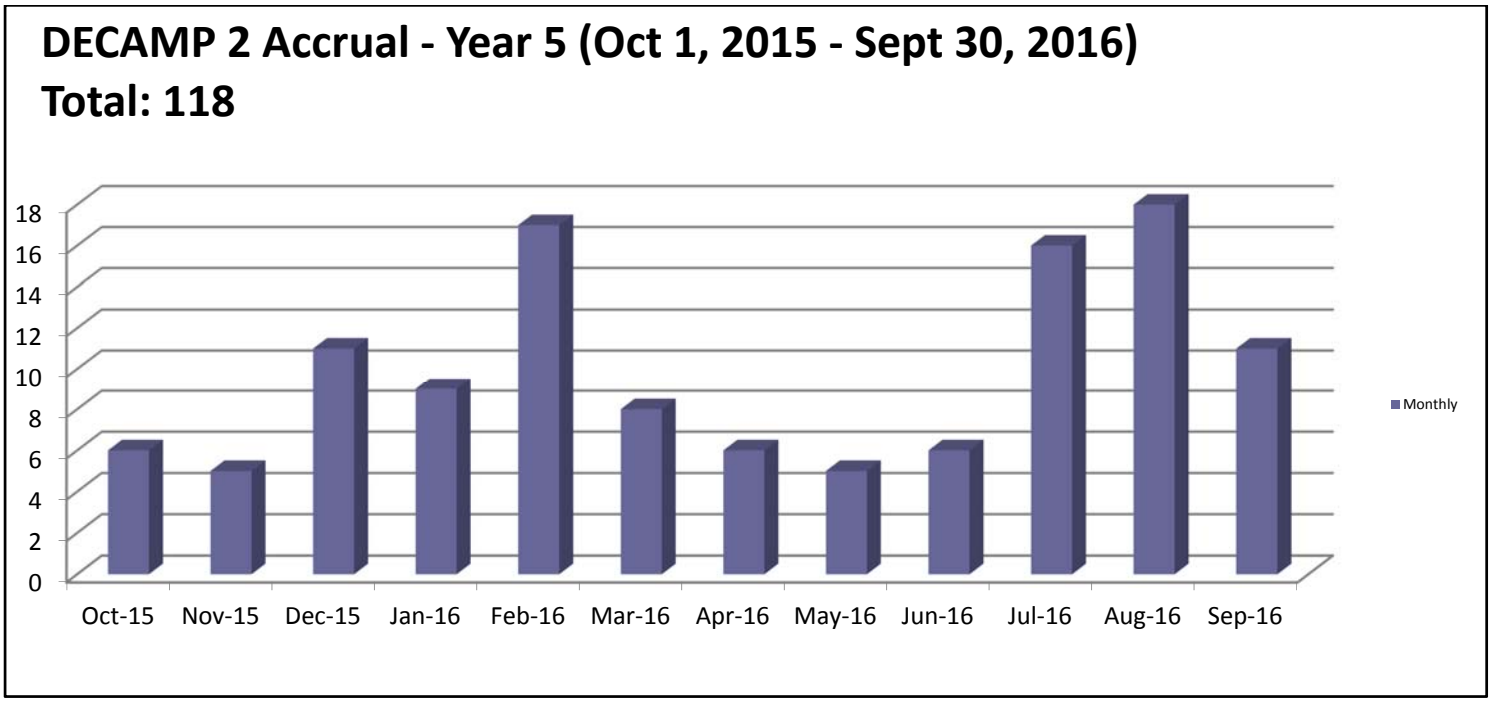


**Table 5: DECAMP-1 Imaging QC**

| Site | Submitted | Qc'd | Missing |
|---|---|---|---|
| 4202 Hospital of the University of Penn | 27 | 27 | 2 |
| 4238 Brooke Army Medical Center | 37 | 37 | 0 |
| 4278 Roswell Park Cancer Institute | 0 | 0 | 0 |
| 4438 VA Los Angeles Healthcare | 20 | 20 | 0 |
| 4714 VA Philadelphia | 16 | 16 | 13 |
| 4790 VA Boston Healthcare | 60 | 60 | 1 |
| 4791 VA North Texas Healthcare | 16 | 16 | 2 |
| 4792 VA Eastern Colorado | 10 | 10 | 0 |
| 4793 VA Nashville Medical Center | 15 | 15 | 0 |
| 4794 VA Pittsburgh Healthcare | 0 | 0 | 12 |
| 4795 Walter Reed National Military MC | 54 | 54 | 6 |
| 4796 Naval Medical Center San Diego | 59 | 50 | 2 |
| 4797 Naval Medical Center Portsmouth | 34 | 34 | 0 |

**Table 6: DECAMP-2 Imaging QC**

| Site | Submitted | Qc'd | Missing |
|---|---|---|---|
| 4202 Hospital of the University of Penn | 12 | 12 | 0 |
| 4238 Brooke Army Medical Center | 10 | 10 | 1 |
| 4278 Roswell Park Cancer Institute | 4 | 3 | 0 |
| 4438 VA Los Angeles Healthcare | 65 | 64 | 10 |
| 4714 VA Philadelphia | 0 | 0 | 0 |
| 4790 VA Boston Healthcare | 37 | 37 | 1 |
| 4791 VA North Texas Healthcare | 1 | 1 | 0 |
| 4792 VA Eastern Colorado | 22 | 22 | 7 |
| 4793 VA Nashville Medical Center | 42 | 42 | 2 |
| 4794 VA Pittsburgh Healthcare | 0 | 0 | 0 |
| 4795 Walter Reed National Military MC | 67 | 61 | 12 |
| 4796 Naval Medical Center San Diego | 83 | 83 | 0 |
| 4797 Naval Medical Center Portsmouth | 43 | 41 | 1 |

## Table 7: DECAMP-1 Table 1

| **Demographic information for DECAMP-1 (n=319)** | | |
|---|---|---|
| Nodule Size | Mean | 1.45 |
| | Range | 0.7-3.0 |
| Age | Median | 68 |
| | Range | 48-89 |
| Gender | Female | 70 |
| | Male | 249 |
| Smoking Status* | Current | 121 |
| | Former | 137 |
| | Missing | 61 |
| Pack Year | Mean | 51.62 |
| | Range | 20-155 |
| COPD** | Yes | 105 |
| | No | 164 |
| | Missing | 50 |
| FEV1%*** | Mean | 74.16 |
| | Range | 3.11-129 |

*Missing data on 61 subjects

**Missing data on 50 subjects

***Missing data on 55 subjects

## Table 8: DECAMP-2 Table 1

| **Demographic information for DECAMP-2 (n=355)** | | |
|---|---|---|
| Age | Mean | 63.55 |
| | Range | 50-79 |
| Gender | Female | 74 |
| | Male | 295 |
| Smoking Status | Current | 142 |
| | Former | 222 |
| Pack Year* | Mean | 49.53 |
| | Range | 20-206 |
| Cigarettes per Day** | Mean | 16.71 |
| | Range | 1-45 |
| COPD*** | Yes | 177 |
| | No | 116 |
| | Missing | 76 |
| FEV1% | Mean | 68.5 |
| | Range | .51-118 |

*For Former Smokers

**For Current Smokers

***missing data on 76 subjects

## Table 9: DECAMP-1 Screening Log

| Site | # CTs Reviewed | # Nodules (total) | # Nodules (eligible) | # Eligible Patients | # Enrolled |
|---|---|---|---|---|---|
| **Boston VA** | 129 | 89 | 28 | 25 | 14 |
| **Dallas VA** | - | - | - | - | 1 |
| **Denver VA** | 257 | 122 | 41 | 41 | 0 |
| **LA VA/UCLA** | 1000 | 280 | 100 | 40 | 6 |
| **Middle TN VA** | 79 | 76 | 29 | 22 | 5 |
| **Philadelphia VA/Upenn** | N/A | 307 | 42 | 28 | 20 |
| **Pittsburgh VA** | - | - | - | - | 0 |
| **Roswell Park** | - | - | - | - | 0 |
| **Brooke Army** | - | - | - | - | 6 |
| **Portsmouth** | 30 | 31 | 6 | 6 | 3 |
| **San Diego** | 149 | 113 | 27 | 9 | 9 |
| **Walter Reed** | - | - | - | - | 15 |
| **Total** | **1644** | **1018** | **273** | **171** | **79** |

## Table 10: DECAMP-2 Screening Logs

| Site | Patients ID'ed | Patients Approached | # Consented |
|---|---|---|---|
| **Boston VA** | 251 | 251 | 15 |
| **Dallas VA** | - | - | 0 |
| **Denver VA** | 99 | 45 | 14 |
| **LA VA/UCLA** | 3248 | 280 | 29 |
| **Middle TN VA** | 96 | 63 | 15 |
| **Philadelphia VA/Upenn** | 1 | 0 | 0 |
| **Pittsburgh VA** | - | - | 0 |
| **Roswell Park** | - | - | 0 |
| **Brooke Army** | - | - | 2 |
| **Portsmouth** | 503 | 414 | 11 |
| **San Diego** | 38 | 24 | 13 |
| **Walter Reed** | - | - | 19 |
| **Total** | **4236** | **1077** | **118** |

Table 11: Biosample Quality and Quantity

| Site | Nasal | | | | | | | Bronch Brush | | | | | | | Bronch Biopsy | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Sample Count | RIN | | | Yield (ug) | | | Sample Count | RIN | | | Yield (ug) | | | Sample Count | RIN | | | Yield (ug) | | |
| | | Avg | Min | Max | Avg | Min | Max | | Avg | Min | Max | Avg | Min | Max | | Avg | Min | Max | Avg | Min | Max |
| 4202 | 4 | 3.5 | 2.8 | 4.8 | 2.74 | 0.02 | 5.7 | 19 | 6.54 | 3.7 | 8.3 | 3.13 | 0.73 | 7.57 | 4 | 4.1 | 2.4 | 6 | 0.7 | 0.06 | 1.29 |
| 4238 | 4 | 4.6 | 2.5 | 10 | 0.26 | 0.16 | 0.4 | 21 | 6.31 | 2.3 | 9.2 | 1.78 | 0.25 | 4.19 | 0 | | | | | | |
| 4278 | 0 | | | | | | | 0 | | | | | | | 0 | | | | | | |
| 4438 | 4 | 4.5 | 2.6 | 7 | 1.66 | 0.44 | 4.37 | 34 | 6.53 | 2.1 | 8.6 | 1.23 | 0.16 | 3.72 | 4 | 3.2 | 2.7 | 3.6 | 0.6 | 0.34 | 1.07 |
| 4714 | 3 | 3.5 | 2.6 | 4.6 | 8.9 | 3.39 | 15.5 | 3 | 4.93 | 2.7 | 7.1 | 6.03 | 4.36 | 8.13 | 4 | 2.9 | 2.2 | 4.5 | 0.88 | 0.46 | 1.29 |
| 4790 | 5 | 4.5 | 2.3 | 7.8 | 6.18 | 1.52 | 11 | 37 | 6.74 | 3.5 | 8.4 | 3.21 | 0.36 | 10.4 | 4 | 4.3 | 1.1 | 7.1 | 1.31 | 0.19 | 2.59 |
| 4791 | 3 | 2.7 | 2.5 | 2.9 | 0.3 | 0.24 | 0.4 | 5 | 5.1 | 2.6 | 6.9 | 2.3 | 0.07 | 4.54 | 3 | 4.9 | 2.5 | 6.7 | 1.38 | 1.09 | 1.94 |
| 4792 | 3 | 6.2 | 4.9 | 7.2 | 7.98 | 1.5 | 14.4 | 5 | 7.98 | 7.2 | 8.9 | 3.97 | 1.01 | 7.07 | 3 | 3.1 | 2.9 | 3.4 | 2.07 | 0.65 | 4.09 |
| 4793 | 4 | 4 | 2.5 | 7.1 | 0.66 | 0.14 | 1.1 | 16 | 5.73 | 2.2 | 7.7 | 2.6 | 0.55 | 5.18 | 4 | 2.6 | 2.2 | 2.8 | 1.3 | 0.71 | 2.77 |
| 4794 | 2 | 4 | 3.3 | 4.7 | 3.52 | 1.93 | 5.12 | 2 | 7.3 | 6.6 | 8 | 4.37 | 4.34 | 4.39 | 3 | 3.5 | 2.6 | 5.2 | 0.62 | 0.06 | 1.31 |
| 4795 | 8 | 4.9 | 2.3 | 7.2 | 6.6 | 0.75 | 12.1 | 63 | 6.33 | 2.3 | 9.4 | 2.46 | 0.24 | 15.4 | 3 | 2.6 | 2.4 | 2.8 | 0.48 | 0.25 | 0.68 |
| 4796 | 8 | 3.3 | 2.3 | 6.3 | 2.65 | 1.11 | 4.89 | 70 | 6.4 | 2.6 | 8.3 | 2.54 | 0.18 | 7.64 | 4 | 2.6 | 2.3 | 2.8 | 0.59 | 0.2 | 1.12 |
| 4797 | 4 | 4.3 | 2.4 | 5.5 | 2.52 | 0.26 | 7.14 | 12 | 6.25 | 4.2 | 8.6 | 2.97 | 1.01 | 6.84 | 4 | 3.2 | 2.4 | 4.9 | 1.25 | 0.58 | 2.15 |
| **All Sites** | **52** | **4.2** | **2.3** | **10** | **3.75** | **0.02** | **15.5** | **287** | **6.4** | **2.1** | **9.4** | **2.53** | **0.07** | **15.4** | **40** | **3.3** | **1.1** | **7.1** | **1** | **0.06** | **4.09** |

## Table 12: Percentage of Subjects (by Site) with at Least One Sample

| Site ID Number | Plasma | Serum | PAXgene | Urine | Buccal | Nasal | Bronch | Biopsy (68) | Biopsy (70) | Biopsy (72) | Sputum |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 4202 | 97% | 97% | 97% | 30% | 80% | 90% | 93% | 87% | 80% | 70% | 0% |
| 4238 | 86% | 92% | 95% | 89% | 24% | 27% | 86% | 0% | 0% | 3% | 11% |
| 4278 | 75% | 75% | 75% | 75% | 75% | 75% | 75% | 75% | 50% | 75% | 75% |
| 4438 | 84% | 82% | 83% | 75% | 83% | 81% | 75% | 71% | 71% | 73% | 42% |
| 4714 | 96% | 96% | 92% | 31% | 77% | 96% | 96% | 77% | 69% | 54% | 0% |
| 4790 | 93% | 92% | 92% | 92% | 93% | 95% | 94% | 86% | 85% | 81% | 76% |
| 4791 | 73% | 73% | 64% | 73% | 73% | 73% | 73% | 73% | 64% | 64% | 55% |
| 4792 | 86% | 86% | 82% | 73% | 86% | 82% | 86% | 86% | 91% | 86% | 73% |
| 4793 | 70% | 70% | 67% | 70% | 60% | 63% | 58% | 49% | 44% | 47% | 63% |
| 4794 | 20% | 20% | 0% | 20% | 20% | 10% | 20% | 20% | 20% | 20% | 90% |
| 4795 | 74% | 77% | 72% | 60% | 80% | 82% | 82% | 70% | 69% | 63% | 59% |
| 4796 | 95% | 93% | 93% | 86% | 91% | 93% | 90% | 72% | 75% | 69% | 51% |
| 4797 | 46% | 49% | 49% | 49% | 46% | 46% | 43% | 35% | 38% | 38% | 59% |

## Table 13: Sample Collection Across All Sites

| | Plasma | Serum | PAXgene | Urine | Buccal | Nasal | Bronch | Biopsy (68) | Biopsy (70) | Biopsy (72) | Sputum |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **N (Subjects with at least one sample)** | 472 | 473 | 464 | 403 | 436 | 449 | 463 | 379 | 372 | 354 | 292 |
| **Total Subjects** | 577 | 577 | 577 | 577 | 577 | 577 | 577 | 577 | 577 | 577 | 577 |
| **% Subjects with Sample** | 82% | 82% | 80% | 70% | 76% | 78% | 80% | 66% | 64% | 61% | 51% |
| **Total Number of Cryovials** | 2769 | 2755 | 954 | 2317 | 456 | 879 | 1515 | 425 | 441 | 446 | 431 |

Table 14: Airway Gene Expression Biomarker Performance Stratified by Nodule Size

| **Nodule Size (cm)** | **All Patients** | **No Cancer (Definite+Leaning)** | **Cancer** | | **Sensitivity** | **Specificity (Definite + Leaning No Cancer)** | **Specificity (Definite No Cancer)** |
|---|---|---|---|---|---|---|---|
| | *no. of patients* | | | | *percent (95% confidence interval)* | | |
| <1 | 21 | 15 | 6 | | 100 (54–100) | 47 (21–73) | 38 (9–76) |
| 1-2 | 57 | 15 | 42 | | 79 (63–90) | 27 (8–55) | 50 (16–84) |
| >2 – 3 | 9 | 1 | 8 | | 88 (47–100) | 100 (3–100) | 100 (3–100) |

**Table 15: DATA COLLECTION Tables as of Oct 11 2016**

Current Database Build Stats

| | # of Unique Folders (Timepoints) | # Unique Forms | # Unique Fields | # of Automatic Validations Programmed | # Updates to DB (since activation of trial) |
|---|---|---|---|---|---|
| DECAMP 1 | 23 | 82 | 1068 | 1413 | 21 |
| DECAMP 2 | 21 | 89 | 1314 | 1415 | 10 |

Case Status

| | Number Enrolled | On Study | Removed Prior to Completion | Completed per Protocol |
|---|---|---|---|---|
| DECAMP 1 | 320 | 221 | 28 | 71 |
| DECAMP 2 | 358 | 321 | 36 | 1 |

Data Collection

| Overall | Total # of Cases | Total Number of Forms Entered | Total Number of Fields Entered | # Queries |
|---|---|---|---|---|
| DECAMP 1 | 320 | 15,730 | 512, 720 | 18, 440 |
| DECAMP 2 | 358 | 18,783 | 737,536 | 22953 |

| | DECAMP 1 | DECAMP 2 |
|---|---|---|
| # of Forms Expected | 16,630 | 24,660 |
| % Overdue | 5.58% | 5.32% |

Data Collection- # of Cases

| | DECAMP 1 | DECAMP 2 Baseline | DECAMP 2 Year 1 | DECAMP 2 Year 2 |
|---|---|---|---|---|
| PFT | 265 | 298 | 120 | 17 |
| Bronchoscopy | 293 | 275 | N/A | 13 |
| CT Image | 293 | 314 | 152 | 17 |
| Blood | 286 | 279 | 101 | 18 |

**DATA COLLECTION as of Oct 11 2016 cont.**

Current Database Build Stats

| | # of Unique Folders (Timepoints) | # Unique Forms | # Unique Fields | # of Automatic Validations Programmed | # Updates to DB (since activation of trial) |
|---|---|---|---|---|---|
| DECAMP 1 | 23 | 82 | 1068 | 1413 | 21 |
| DECAMP 2 | 21 | 89 | 1314 | 1415 | 10 |

Case Status

| | Number Enrolled | On Study | Removed Prior to Completion | Completed per Protocol |
|---|---|---|---|---|
| DECAMP 1 | 320 | 221 | 28 | 71 |
| DECAMP 2 | 358 | 321 | 36 | 1 |

Data Collection

| Overall | Total # of Cases | Total Number of Forms Entered | Total Number of Fields Entered | # Queries |
|---|---|---|---|---|
| DECAMP 1 | 320 | 15,730 | 512, 720 | 18, 440 |
| DECAMP 2 | 358 | 18,783 | 737,536 | 22953 |

| | DECAMP 1 | DECAMP 2 |
|---|---|---|
| # of Forms Expected | 16,630 | 24,660 |
| % Overdue | 5.58% | 5.32% |

Data Collection- # of Cases

| | DECAMP 1 | DECAMP 2 Baseline | DECAMP 2 Year 1 | DECAMP 2 Year 2 |
|---|---|---|---|---|
| PFT | 265 | 298 | 120 | 17 |
| Bronchoscopy | 293 | 275 | N/A | 13 |
| CT Image | 293 | 314 | 152 | 17 |
| Blood | 286 | 279 | 101 | 18 |

Key Research Accomplishments:

Poster Presentations:
Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. Detection and validation of molecular biomarkers for the early detection of lung cancer among military and veteran populations: The DECAMP consortium. Oral Presentation presented at the American Thoracic Society Conference; 2015 May; Denver, CO.

Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. Airway gene-expression in the DECAMP consortium as a molecular window into COPD and lung cancer. Oral Presentation presented at American Association of Bronchology and Interventional Pulmonology Research Symposium; 2014 October; Austin, TX.

Jiwani, A. Z., Maple, E., Mahon, I., Apgar, C., Atwood, C.W., Battaile, J.T., Browning Jr., R., Garshick, E., Goldstein, R.H., Keith, R.L., More, K., Morris, M.J., Parrish, J.S., Reid, M., Vachani, A., Gatsonis, C., Elashoff, D., Duan, F., Dubinett, S.M., Lenburg, M., Massion, P.P., Remick, D.G., Wistuba, I.I., Schnall, M., and Spira, A. (2014, October). Detection and validation of molecular biomarkers for the early detection of lung cancer among military and veteran populations: The DECAMP consortium. Oral Presentation presented at: American College of Chest Physicians Conference; 2014 October; Austin, TX.

Billatos E, Muse M, Jiwani A, Mahon I, Maple E, Atwood C.W., Apgar C, Battaile J.T., Browning R, Garshick E, Goldstein R.H., Keith R.L., More K, Morris M, Parrish J.S., Reid M, Gatsonis C, Elashoff D, Duan F, Dubinett S.M., Lenburg M, Massion P.P., Remick D, Wistuba I.I., Schnall M, Vachani A, Spira A. Diagnostic Evaluation of the Indeterminate Pulmonary Nodule Among Military and Veteran Personnel with Suspect Lung Cancer: The DECAMP Consortium. Oral Presentation presented at: American Thoracic Society; 2016 May 13-18; San Francisco, CA.

E. Billatos, E. Maple, I. Mahon, C. Apgar, C. W. Atwood, J. T. Battaile, R. Browning, E. Garshick, R. H. Goldstein, A. Vachani, R. L. Keith, K. More, M. Morris, J. S. Parrish, M. Reid, C. Gatsonis, D. Elashoff, F. Duan, S. M. Dubinett, M. Lenburg, P. P. Massion, D. Remick, I. I. Wistuba, M. Schnall, A. Spira. Diagnostic Evaluation of the Indeterminate Pulmonary Nodule Among Military and Veteran Personnel with Suspect Lung Cancer: The DECAMP Consortium. Oral Presentation presented at: Evans Day; 2016 Oct 13; Boston, MA.

Publications:
Silvestri, G. A., et al. (2015). A Bronchial Genomic Classifier for the Diagnostic Evaluation of Lung Cancer. *N Engl J Med,* 373, 243-51.

Reportable Outcomes:
n/a

Conclusion:
Overall, we have made significant progress towards accomplishing the goals of this consortium over the past 12 months. Recruitment of subjects into both clinical trials has continued to improve steadily and follow-up visits for DECAMP-2 are increasing. We are improving communication within the consortium through the formation of designated committees to support imaging and biostatistical analyses. Most importantly, we have begun validation on two biomarkers from bronchial brushings and from blood. We are confident that this momentum will continue through the no cost extension.